

## **MECHANICAL STRESS AND ANTIOXIDANT PROTECTION IN THE RETINA OF HINDLIMB SUSPENDED RATS**

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It has been postulated that hindlimb suspension (HS) causes a cephalad fluid shift in quadrupeds similar to that occurring to humans in microgravity. Therefore, HS may provide a suitable animal model in which to recapitulate the ocular changes observed in the human Visual Impairment and Intracranial Pressure (VIIP) syndrome. This work reports preliminary results from a tissue sharing project using 34 week-old Brown Norway rats. Two different experiments compared normal posture controls and HS rats for 2 weeks and rats exposed to HS for 2 weeks but allowed to recover in normal posture for 2 additional weeks. The effects of two nutritional countermeasures, green tea extract (GT) and plant polyphenol resveratrol (Rv), were also evaluated. Green tea contains the antioxidant epigallocatechin gallate (EGCG). qPCR gene expression analysis of selected targets was performed on RNA from isolated retinas, and histologic analysis was done on one fixed eye per rat. The transcription factor early growth response protein 1 (Egr1) was upregulated almost 2-fold in HS retinas relative to controls ( $P = 0.059$ ), and its expression returned to control levels after 2 weeks of recovery in normal posture ( $P = 0.023$ ). HS-induced upregulation of Egr1 was attenuated (but not significantly) in retinas from rats fed an antioxidant rich (GT extract) diet. In rats fed the GT-enriched diet, antioxidant enzymes were induced, evidenced by the upregulation of the gene heme oxygenase 1 (Hmox1) ( $P = 0.042$ ) and the gene superoxide dismutase 2 (Sod2) ( $P = 0.0001$ ). Egr1 is a stretch-activated transcription factor, and the Egr1 mechanosensitive response to HS may have been caused by a change in the translaminal pressure and/or mechanical deformation of the eye globe. The observed histologic measurements of the various retinal layers in the HS rats were lower in value than those of the control animal ( $n = 1$ ), however insufficient data were available for statistical analysis. Aquaporin 4, a water-selective channel involved in interstitial fluid homeostasis, showed an upregulated trend in HS retinas; however, these results are preliminary. Total retinal thickness increased significantly ( $P = 0.049$ ) in HS rats fed a resveratrol enriched diet compared to HS rats on a normal diet. This change appeared to be reversed during the 2 weeks of recovery post HS, but no differences in retina thickness were observed between HS animals and HS recovered animals when both groups consumed a normal diet. The reversibility of the increase in retinal thickness induced by resveratrol during HS may therefore reflect an interaction between the stress provoked by HS and the cytoprotective mechanisms elicited by resveratrol.